Development of a novel space flight plan to monitor female mice fertility using reduced crew time.

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Ovarian estrogen impacts the normal homeostatic and metabolic processes of all tissues and organ systems within the body: particularly, but not limited to canonical space-flight impacted systems: bone, muscle, immune, wound repair, and cardiovascular. Effects of space flight on the ovarian estrogen production are therefore critical to our understanding of all space flight experiments using female mice, the current paradigm being used on the International Space Station (ISS). Recently, we demonstrated that vaginal wall histology could be used to determine the stage of the estrous cycle in female mice at the time of sacrifice in space. Moreover, this robust technique was completed following two post-flight freeze/thaw procedures of the carcasses (RR1 experiment). Thus, this technique represents a viable mechanism to determine the estrous cycle status of the female at the time of sacrifice and can be completed in a manner that does not impact primary experimental objectives. We propose that vaginal wall histology become a standard procedure completed on all mice sacrificed in space and that the individual estrous status of each animal be shared with all investigators. While evidence of estrous cyclicity was present in long-term (33 day) RR1 mice, fertility of female mice exposed to weightlessness remains unknown. In preparation for an upcoming funded NASA flight investigating the effects of long duration spaceflight on female fertility, we have refined our experimental design to minimize crew ~~flight~~ time and to accommodate the duration of Dragon capsule berth. These refinements maintain all our proposed primary and secondary experimental objectives. Briefly, in order to evaluate fertility, we will super ovulate mice using standard procedures (PMSG ± hCG), followed by collection of reproductive tract after follicular stimulation alone (PMSG) or following ovulation (hCG). Ovarian folliculogenesis and ovulation rate will be determined in fixed tissues following return in order to determine fertility. Ovarian and uterine tissues will also be evaluated by hormonal and gene expression profiling using quantitative approaches (radioimmunoassays, western blots, digital droplet PCR). Comparisons will be made to contemporary vivarium and Rodent Research Hardware –Transporter and Habitat housed animals maintained on earth. Supported by NNX15AB48G to JST.